## AMENDMENTS TO THE SPECIFICATION

**IN THE SPECIFICATION:**

Before line 1 of the specification, please insert the following new paragraph:

This application is a Divisional of co-pending Application No. 09/786,681, filed on April 30, 2001, the entire contents of which are hereby incorporated by reference and for which priority is claimed under 35 U.S.C. § 120; and this application claims priority of Application No. 253771/1998 filed in Japan on September 8, 1998, under 35 U.S.C. § 119.

Please replace the paragraph beginning at page 1, line 24 and ending on page 2, line 10 with the following amended paragraph:

SM-11044 ((L)-threo-3-(3,4-dihydroxyphenyl)-N-[3-(4-fluoro phenyl)propyl] serine pyrrolidine amide hydrobromide)-binding receptor protein (SMBP) was discovered as a new protein that is bound by SM-11044, which is an agonist for β-adrenergic receptors, and by iodocyanopindolol, which is an antagonist for β-adrenergic receptors (Sugasawa, T. et al., J. Biol. Chem. ~~267~~ 272, 21244-21252 (1997)). SMBP is a membrane protein resided at lung, ileum, and eosinophil membrane, and is believed to act as a receptor for SM-11044. SM-11044 was known to have activities to down-regulate the

depolarization-mediated contraction of intestine and to inhibit migration of eosinophils, and has been believed to exert such SM-11044's functions via SMBP (Sugasawa, T. et al., J. Biol. Chem., 272, 21244-21252 (1997)).

Please replace the paragraph on page 10, lines 18-25 with the following amended paragraph:

Examples of the method for measuring a ligand-binding activity include the method described in *J.Biol.Chem.*, ~~267~~ 272, 21244-21252 (1997). The method in principle comprises determining a binding reactivity to 1nM [$^{125}$I]-iodocyanopindolol used as a ligand, determining a nonspecific binding reactivity of iodocyanopindolol by use of $10^{-4}$ M SM-11044, and subtracting the nonspecific binding reactivity from the binding reactivity so as to measure a ligand-binding activity of SMBP protein (J. Biol. Chem., ~~267~~ 272, 21244-21252 (1997)).

Please replace the paragraph beginning at page 10, line 26 and ending on page 12, line 6 with the following amended paragraph:

Specifically, a human SMBP expression vector is prepared by introducing a candidate DNA for the DNA of the present invention into an expression vector, and a transformed cell is prepared by introducing the SMBP expression vector into a host cell. Then, the resultant transformed cells or cellular membrane fractions thereof

are subjected to the system for measuring a ligand-binding activity as shown above (the expression vector, the transformed cells, and the cellular membrane fractions thereof are further described hereinafter). Examples of the method for measuring a ligand-binding activity include the substantially same method as that described in *J. Biol. Chem.*, ~~267~~ 272, 21244-21252 (1997) mentioned above, and a method that is detailed in Example 6. Specifically, a 96-well Multiscreen plate (Millipore) in which a piece of glass fiber paper is placed on the bottom of the wells is treated with Tris-HCl buffered saline containing 0.3% polyethyleneimine (Sigma) (reconstituted to pH7.4 with 6N HCl), and washed by vacuum filtration with Tris-HCl buffered saline (pretreatment). Then, 200 $\mu$l of Tris-HCl buffered saline containing 1nM [$^{125}$I]-iodocyanopindolol (Amersham) and a cellular membrane fraction as mentioned above (50 $\mu$g of membrane protein) that have been incubated at 37°C for 30 minutes is added to each well on the 96-well Multiscreen plate, and are washed by vacuum filtration. The cellular membrane fraction is harvested on the glass fiber paper, and washed by vacuum filtration with 200 $\mu$l of an ice-cooled Tris-HCl buffered saline. Then, the amount of [$^{125}$I]-iodocyanopindolol bound to the membrane fraction trapped on the paper is determined by a gamma counter to represent a total binding. Nonspecific binding of [$^{125}$I]-iodocyanopindolol is determined by conducting an incubation as mentioned above in the presence of $10^{-4}$ M SM-11044

(Sumitomo Pharmaceuticals Co., Ltd. it can be prepared according to the process described in Japanese Patent Publication (kokai) No. 132935/1985, Japanese Patent Publication (kokoku) No. 50499/1993) and then conducting similar procedures to those mentioned above. A ligand-binding to SMBP may be calculated by subtracting the nonspecific binding from the total binding.

Please replace the paragraph beginning at page 16, line 3 and ending on page 17, line 3 with the following amended paragraph:

First of all, a Tris-HCl buffered saline containing the cellular membrane fraction of the present invention (50-200 μg membrane protein) and 1nM [$^{125}$I]-iodocyanopindolol is incubated at 37°C for 30 minutes, and the reaction is added to each well on a ~~96 well~~ 96-well Multiscreen plate that has been treated by a similar pretreatment to that in "the method for measuring a ligand-binding activity" as mentioned above, then being aspirated by vacuum filtration. Subsequently, a similar treatment to that in "the method for measuring a ligand-binding activity" as mentioned above is conducted, and the amount of [$^{125}$I]-iodocyanopindolol bound to the membrane fraction trapped on the paper is determined by a gamma counter to give a binding, which represents binding A. Then, the incubation as shown above is conducted in the presence of a test compound at a normal ~~rage~~ range of concentrations ($10^{-12}$-$10^{-4}$M), and then a similar procedure is conducted to give a binding, which

represents binding B. A binding that is provided by use of $10^{-4}$M SM-11044 instead of a test compound represents binding C. Accordingly, when the value subtracted binding B from binding A is equivalent to one subtracted binding C from binding A, the test compound is estimated to have 100% SMBP-binding activity, and, when the value is the half, the compound is estimated to have the 50%. SMBP ligands thus selected are subjected to an assay as described in either *J. Biol. Chem.*, ~~267~~ 272, 21244-21252 (1997), *Eur. J. Pharmacol.* 216, 207-215 (1992), or *Agents Actions* 37, 233-237 (1992). At that time, when down-regulating the contraction of intestine or inhibiting the migration of eosinophils equivalently to or more than SM-11044, the ligands may be a SMBP agonist, whereas when showing the inverse activities, they may be a SMBP antagonist.

Please replace the paragraph beginning at page 21, line 25 and ending on page 22, line 5 with the following amended paragraph:

In surrounding sequences of ATG, a start codon, of the SMBP-cDNA fragment (at positions 49-51 in SEQ ID NO: 1), the Kozak's consensus sequence (ACCATGG SEQ ID NO:5) presumed to be necessary to translate efficiently mRNAs into proteins is not found. Accordingly, the surrounding sequence of the start codon of SMBP-cDNA fragment was replaced with ACCATGG (SEQ ID NO:5) as shown below in order to improve expression efficiency of proteins.

Please replace the text at page 22, lines 10 and 11 with the following amended text:

5'-AGC TTC CAC CAT GGC-3' (SEQ ID NO: 6)

3'-AG GTG GTA CCG CCG G-5' (SEQ ID NO: 7)

Please replace the paragraph at page 26, lines 11-21 with the following amended paragraph:

Sugasawa et al. (Sugasawa, T. et al., *J. Biol. Chem.*, ~~267~~ 272, 21244-21252 (1997)) reported that a ligand-binding reactivity of a human SMBP protein can be measured by use of 1nM [$^{125}$I]-iodocyanopindolol (2000 Ci/mmol; Amersham) as a ligand, and, specifically, the ligand-binding reactivity of a human SMBP protein can be estimated by determining a nonspecific binding reactivity of iodocyanopindolol by use of $10^{-4}$M SM-11044, and subtracting the non-specific binding reactivity from the binding reactivity. According to the instructions of this literature, a ligand-binding activity of a SMBP protein was measured. Further, the binding assay was conducted using a 96-well microtiter plate in order to accelerate the assay.

Please replace the paragraph beginning at page 28, line 11 and ending on page 29, line 9 with the following amended paragraph:

Two hundreds μl of Tris-HCl buffered saline containing 50 μg of membrane protein of the cellular membrane fraction of the CHO cells transformed with SMBP-Kozak-pcDNA3.1/Zeo(+) poly-T free (as prepared in Example 5) and 1nM [$^{125}$I]-iodocyanopindolol is incubated at 37°C for 30 minutes, and the reaction is added to each well on a ~~96-well~~ 96-well Multiscreen plate that has been treated by a similar pretreatment to that in Example 6, and aspirated by vacuum filtration. Then, a similar treatment to that ~~that~~ in Example 6 is conducted, and the amount of [$^{125}$I]-iodocyanopindolol bound to the membrane fraction trapped on the paper is determined by a gamma counter to give a binding, which represents binding A. Subsequently, the incubation as shown above is conducted in the presence of a test compound at a normal ~~rage~~ range of concentrations ($10^{-12}$-$10^{-4}$M), and then a similar procedure is conducted to give a binding, which represents binding B. A binding that is provided by use of $10^{-4}$M SM-11044 instead of a test compound represents binding C. When the value subtracted binding B from binding A is equivalent to one subtracted binding C from binding A, the test compound is estimated to have 100% SMBP-binding activity, and, when the value is the half, the compound is estimated to have the 50%. SMBP ligands thus selected are subjected to an assay as described in either *J. Biol. Chem.*, ~~267~~

272, 21244-21252 (1997), *Eur. J. Pharmacol.* 216, 207-215 (1992), or *Agents Actions* 37, 233-237 (1992). That procedure makes it possible to determine if the ligands have a SMBP-agonist activity, i.e., if the ligands down-regulate the contraction of intestine or if they inhibit the migration of eosinophils.